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PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

TANAKA, Akiko; JESSIP, John; and BRADLEY, William Guy

Application No.: 09/964,240

Art Unit: 1654

Filed: September 26, 2001

Examiner: TATE, C.

For: PINE CONE EXTRACTS AND USES THEREOF

Conf. No.: 1854

Attorney Docket: 3974.002

DECLARATION UNDER 37 C.F.R. §1.131

Mail Stop Non-Fee Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, William Guy BRADLEY, of 10900 Roosevelt Blvd., St. Petersburg, Florida 33716-2308, declare and state as follows:

1. I am a co-inventor of the invention disclosed and claimed in the above-identified application for U.S. Patent, am familiar with the contents of the Office Action mailed in regard to said application on March 24, 2003, and submit this Declaration for the purpose of establishing a date of invention prior to the date of publication of the reference Xin (CN 1279107), which is cited in said Office Action.

2. I was awarded a Ph.D. in Medical Science from the University of South Florida, College of Medicine, Department of Microbiology and Immunology, was previously Associate Professor of Molecular Physiology at Eckerd College, Florida, and am

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currently employed as an Associate Member and Principal Investigator at the Tampa Bay Research Institute, St. Petersburg, Florida.

3. Prior to June 1, 1999, as the result of a collaboration between Akiko TANAKA, William Guy BRADLEY, and John JESSIP, (herein collectively "we"), I contributed to conception of the subject invention as disclosed and claimed in the above-captioned application for U.S. Patent.

4. On June 1, 1999, and in part as a result of the collaboration described in paragraph 4, a proposal for research funding naming William Guy BRADLEY, Ph.D., as Principal Investigator, and titled "Dissecting the Legendary Anti-Tumor Activity of a Pine Complex: Activating the Anti-Tumor Potential of Macrophage and Dendritic Cells," was submitted to the U.S. Army Medical Research and Materiel Command, and that a copy of this proposal and accompanying letter of submission is appended as Appendix A.

5. Receipt of the proposal of Appendix A was acknowledged by mail in the form of a postcard, a copy of which is appended as Appendix B, which postcard was mailed by the office of Dr. Kenneth A. Bertram, Lt. Col., U.S. Army Medical Corps, to Dr. William G. Bradley, assigning identification number BC990863 to the proposal.

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6. The proposal of Appendix A sets forth, as described below, the essence of the invention of the above-captioned application for U.S. patent.

7. I was aware from prior studies that activation of dendritic cells in vitro in the presence of tumor antigen and specific cytokines can induce tumor-specific cytotoxicity when the dendritic cells thus treated are used as a tumor vaccine. See Appendix A at page 8, lines 4-5.

8. In the proposal of Appendix A, we proposed the hypothesis that the host-mediated anti-tumor activity of pinecone extract resides in its ability to alter immune function in favor of a Th1 response, and in its ability to activate dendritic and macrophage cells. See Appendix A at p. 10, lines 3-6.

9. I understood at the time of filing the grant application of Appendix A (June 1, 1999) that the only known function of dendritic cells was to present antigen to T-cells, and that the mature dendritic cells found in lymphoid tissues were generally known to be by far the most potent stimulators of naïve T cells. See Janeway "The Immune System in Health and Disease" 5th Edn., Garland Publishing, at p.307, §8-6, and Appendix A at p.7, ¶¶3-5, et seq.

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10. It was my belief and opinion at the time of filing the proposal of Appendix A on June 1, 1999, that an agent which boosted dendritic cell function would also boost antigen presentation to T-cells, which is precisely the function of a vaccine adjuvant. See Janeway at p.576 ("The potency of dendritic cells in activating T-cell responses provides the rationale provides the rationale for yet another strategy for vaccinating against tumors. The use of antigen-pulsed autologous dendritic cells to stimulate therapeutically useful T-cell responses to tumors has been developed in experimental models, and there have been initial trials in humans with cancers," and Appendix A at p.7, ¶¶3-5 et seq.

11. It was my belief and opinion at the time of filing the proposal of Appendix A that elucidation of the mechanism of action of PC extract would aid in the use of pine cone extract to complement current anti-cancer therapies.

12. We demonstrated in a pilot study prior to the time of filing the proposal of Appendix A that oral delivery of pine cone extract to aged mice reduced the incidence of spontaneous tumor formation, consistent with our hypothesized mechanism of action of pine cone extract. See Appendix A at p.9, ¶5.

13. We proposed experiments in the proposal of Appendix A to test our hypothesis that exposure of murine dendritic cells to pine cone extract in vitro will prime the cells for anti-tumor activity in vivo. See Appendix A at p.5.

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14. Thus, I declare that as of the date of submission of the proposal (June 1, 1999) we had conceived and were in possession of the invention as disclosed and claimed in the subject application for U.S. Patent, and were actively engaged in its reduction to practice.

15. That reduction to practice of the invention continued diligently from prior to the filing of the proposal of Appendix A to the filing of the above-captioned application for U.S. Patent, as shown by the statement of financial support provided by Ms. Diane Tippins, Business Manager of the Tampa Bay Research Institute, a copy of which is appended as Appendix C.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of this application or any patent issuing thereon.

Date: July 29, 2003

William Guy Bradley
William Guy BRADLEY, Ph.D.